

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
3 June 2004 (03.06.2004)

PCT

(10) International Publication Number  
**WO 2004/046160 A3**

(51) International Patent Classification<sup>7</sup>: **A61K 31/7088**,  
C07H 21/00

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(21) International Application Number:  
PCT/DK2003/000788

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(22) International Filing Date:  
18 November 2003 (18.11.2003)

(81) Designated States (*national*): AE, AG, AL, AM, AT (util-  
ity model), AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,  
CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE  
(utility model), DE, DK (utility model), DK, DM, DZ, EC,  
EE (utility model), EE, EG, ES, FI (utility model), FI, GB,  
GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,  
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,  
MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL,  
PT, RO, RU, SC, SD, SE, SG, SK (utility model), SK, SL,  
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,  
YU, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
PA 2002 01774 18 November 2002 (18.11.2002) DK  
PA 2003 01540 20 October 2003 (20.10.2003) DK

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(84) Designated States (*regional*): ARIPO patent (BW, GH,  
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,  
SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,  
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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**Published:**

- with international search report
- before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

(88) Date of publication of the international search report:  
21 October 2004

*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: AMINO-LNA, THIO-LNA AND ALPHA-L-OXY-LN

(57) Abstract: A novel class of pharmaceuticals which comprises a Locked Nucleic Acid (LNA) which can be used in antisense therapy. These novel oligonucleotides have improved antisense properties. The novel oligonucleotides are composed of at least one LNA selected from beta-D-thio/amino-LNA or alpha-L-oxy/thio/amino-LNA. The oligonucleotides comprising LNA may also include DNA and/or RNA nucleotides.

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK 03/00788

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61K31/7088 C07H21/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ, MEDLINE, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KUMAR RAVINDRA ET AL: "The first analogues of LNA (locked nucleic acids): Phosphorothioate-LNA and 2'thio-LNA" BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 8, no. 16, 18 August 1998 (1998-08-18), pages 2219-2222, XP002281372 ISSN: 0960-894X cited in the application page 2221; table 1	1-31, 39-42
A	---	32-38
	-/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

24 May 2004

Date of mailing of the international search report

30 AUG 2004

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK 03/00788

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SINGH S K ET AL: "SYNTHESIS OF 2'-AMINO-LNA: A NOVEL CONFORMATIONALLY RESTRICTED HIGH-AFFINITY OLIGONUCLEOTIDE ANALOGUE WITH A HANDLE" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY, EASTON, US, vol. 63, no. 26, 1998, pages 10035-10039, XP002901079 ISSN: 0022-3263 cited in the application page 10037; table 1	1-31, 39-42
A	---	32-38
X	WO 01 48190 A (EXIQON AS ;KOCH TROELS (DK); ORUM HENRIK (DK); SKOUV JAN (DK); JAK) 5 July 2001 (2001-07-05) page 5, line 21 -page 6, line 5 page 10, line 28,14-31 page 36, line 6 - line 24	1-31, 39-42
A	---	32-38
X	SORENSEN MAD S D ET AL: "alpha-L-ribo-configured locked nucleic acid (alpha-L-LNA): Synthesis and properties" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 124, no. 10, 13 March 2002 (2002-03-13), pages 2164-2176, XP002281373 ISSN: 0002-7863 page 2168 page 2170, left-hand column, paragraph 3 -page 2171, right-hand column, paragraph 1; figure 3	1-9, 22-31, 39-42
A	---	32-38
X	KEINICKE LISE ET AL: "alpha-L-RNA (alpha-L-ribo configured RNA): Synthesis and RNA-selective hybridization of alpha-L-RNA/alpha-L-LNA chimera" BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 12, no. 4, 25 February 2002 (2002-02-25), pages 593-596, XP002281374 ISSN: 0960-894X page 594; table 1 page 595, right-hand column, paragraph 3 abstract	1-9, 22-31, 39-42
A	---	32-38
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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK 03/00788

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 66604 A (EXIQON AS ;WENGEL JESPER (DK)) 9 November 2000 (2000-11-09) page 9, line 20 - line 30 page 18, line 20 - line 24 page 19, line 20 -page 20, line 28 page 21, line 10 - line 26 page 35, line 6 - line 35 page 33, line 5 - line 8 page 37, line 6 - line 8	1-31, 39-42
A	---	32-38
X	WO 01 25478 A (EXIQON AS ;KOSHKIN ALEXEI (DK); JAKOBSEN MOGENS HAVSTEEN (DK)) 12 April 2001 (2001-04-12) page 4, line 14 -page 6, line 8 page 12, line 4 - line 15 page 9, line 17 -page 10, line 11 page 26; claim 28	32-39
A	---	1-31, 39-42
X	KURRECK JENS ET AL: "Design of antisense oligonucleotides stabilized by locked nucleic acids" NUCLEIC ACIDS RESEARCH, vol. 30, no. 9, 1 May 2002 (2002-05-01), pages 1911-1918, XP002281375 ISSN: 0305-1048 page 1912, left-hand column; table 1 page 1916 -page 1917 discussion	32-38
A	---	1-31, 39-42
X	WO 01 25248 A (EXIQON AS ;JAKOBSEN MOGENS HAVSTEEN (DK); WAHLESTEDT CLAES (SE)) 12 April 2001 (2001-04-12) page 3, line 1 -page 11 page 4, line 4 -page 12 page 6, line 18 -page 7, line 14 page 8, line 16 -page 9, line 25 page 13; claim 8	32-38
A	---	1-31, 39-42
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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK 03/00788

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>FRIEDEN MIRIAM ET AL: "Expanding the design horizon of antisense oligonucleotides with alpha-L-LNA." NUCLEIC ACIDS RESEARCH, vol. 31, no. 21, 1 November 2003 (2003-11-01), pages 6365-6372, XP002281376 ISSN: 0305-1048 (ISSN print) page 6367, left-hand column, paragraph 2; table 1 page 6369, right-hand column -page 6371 -----</p>	<p>1-9, 22-42</p>

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/DK 03/00788

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-31,32-38

Claims: 1-31, 32-38 (when the claims relate to amino-LNA, thio-LNA or alpha-L-oxy-LNA-containing nucleotides) and 39-42, directed to pharmaceutical compositions and oligonucleotide constructs comprising amino-LNA, thio-LNA or alpha-L-oxy-LNA

2. Claims: 32-38

Claims 32-38 directed to oligonucleotide constructs of the formula A-B-C-D (A, C: LNA, B, D non-locked nucleotide units)

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 03/00788

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0148190	A	05-07-2001	AU 3041701 A	09-07-2001
			CA 2395320 A1	05-07-2001
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			EP 1224280 A2	24-07-2002
			JP 2003511016 T	25-03-2003
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